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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/760,506	01/12/2001	Charlotte Kensil	8449-153	2171
20583	7590	11/04/2005	EXAMINER	
JONES DAY 222 EAST 41ST ST NEW YORK, NY 10017			QIAN, CELINE X	
			ART UNIT	PAPER NUMBER
			1636	

DATE MAILED: 11/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/760,506

Applicant(s)

KENSIL, CHARLOTTE

Examiner

Celine X. Qian Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 13 September 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 31 and 33-387 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 31, 33-38, 40 and 44-54 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 12 January 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |                                                                                                                        |                                                                                         |
|------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                                                       | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____                                                |

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### **DETAILED ACTION**

Claims 31, 33-38, 40, 44-54 are pending in the application.

This Office Action is in response to the Amendment filed on 9/13/05.

#### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/13/05 has been entered.

#### ***Response to Amendment***

The rejection of claims 31, 33-38, 40, 44-54 under 35 U.S.C. 112 1<sup>st</sup> paragraph is maintained for reasons set forth of the record mailed on 1/13/05 and further discussed below.

#### ***Response to Arguments***

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 31, 33-38, 40, 44-54 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inhibiting tumor growth comprising administering to an individual an effective amount of a composition comprising *Quillaja saponaria* saponin to the vicinity of the tumor or intravenously, wherein said composition stimulates innate immunity, and wherein said composition does not contain a vaccine antigen,

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with or without an oligonucleotide that comprises unmethylated CpG, does not reasonably provide enablement for a method of treating cancer comprising administering to an individual in need thereof an effective amount of a composition comprising a *Quillaja saponaria* saponins by any other route, or a composition comprising any chemically modified form of said *Quillaja saponaria* saponins. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In response to this rejection, Applicants argue that the claims are enabled to full scope because undue experimentation is not required to practice the method as claimed. Applicants argue that inhibiting tumor is a form of cancer treatment, wherein patient will greatly benefit if the tumor does not increase in size. Applicants argue that inhibiting tumor may prevent or delay a tumor from becoming metastatic or delay disease progression. Applicants thus conclude that delaying tumor growth and progression is sufficient to be an effective cancer treatment.

Applicants further argue that *in vivo* mouse model are reasonably predictive of the success of these compounds for treating cancer in human according to *In re Brana* and MPEP. Moreover, Applicants submitted a Declaration by Dr. Clynes which demonstrate intravenous administration of QS-21 inhibited tumor growth in the mouse, and assert that such data enables the claimed method for administration other than intratumorally administration. Furthermore, Applicants argue that the second Kensil Declaration state that *Quillaja saponaria* saponins share a common structure that gives rise to the common innate immunity function, and would be expected to function in the same manner with respect to treat cancer. Applicants argue that the declaration also teaches what modification can be made without affecting innate immunity, whereas the first

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Kensil declaration demonstrate that QS saponins can treat cancer. Applicants thus conclude that based on such art recognized connection of innate immunity and cancer, the claimed method is enabled to the full scope.

The above arguments have been considered and deemed partially persuasive. The examiner accepts that the method of inhibiting tumor growth is enabled for intravenous administration of QS saponins as well as intratumoral administration, and the claimed method is enabled to the scope as indicated above. However, the claims are not enabled for a method of treating cancer by any other chemically modified form of QS saponins for same reasons as discussed in the previous office actions. In response to Applicants argument with regard to treating cancer, Applicants are reminded that there is a difference between inhibiting a tumor in a mouse which is transplanted with a tumor and achieve a therapeutic effect for treating cancer in human. As discussed in the office action mailed on 4/20/04, mouse models used in testing anti-tumor agent are often faulty as discussed in the Gura article (see page 5). A naturally occurring tumor in human may behave very differently from the tumor that is inoculated in the mouse. Further, cancer is not limited to solid tumor. Moreover, a therapeutic effect of treating cancer would encompass alleviate of the patient condition, not simply delay tumor progression. Furthermore, neither the specification nor any data submitted by Applicant demonstrates that said QS saponins actually delay or prevent metastasis in human. As such, while the claimed method is enabling for a method of inhibiting tumor growth, it is not enabled for a method of treating cancer.

In response to Applicant's argument with regard to *In re Brana*, the examiner already pointed out the difference between the claimed invention in the *Brana* case and the instant

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invention in the previous office action (see page 5 of the office action mailed on 1/13/05). The examiner reiterates that this case law does not support the enablement of the instant claims because the standard is different in these cases, wherein the claimed invention is chemical compound in *Brana*, whereas the claimed invention is a method of treating cancer in the instant application. Further, the examiner does not agree that the QS compounds provided in the second Kensil declaration would function in same manner when used to treat cancer. While the second declaration addresses innate immunity, it does not extend the predictability to therapeutic effect in treating cancer in human for reasons discussed in the previous office action and above. If Applicant's assertion that a correlation between innate immunity and inhibition of tumor growth in mouse is sufficient for the enablement a method of treating cancer in human, Applicants are reminded that the Chavali reference cited in office action mailed on 10/23/02 would have disclosed, or at least given sufficient motivation to make the claimed invention because it discloses a method of enhance innate immunity in a mouse by administering the QS saponin. Applicant's attention is directed to the response filed on 4/23/03, wherein Applicant argues that enhancement of innate immune response is not obvious for treating cancer. Applicant's previous arguments appear contradictory to the arguments presented above. The examiner reiterate the position that whether any chemically modified QS saponin can treat cancer is unpredictable. Therefore, the claimed invention is only enabled to the scope indicated above. The rejection is maintained.

### ***Double Patenting***

Applicant is advised that should claims 35, 36 and 53 be found allowable, claims 47, 48 and 54 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two

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claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X. Qian Ph.D. whose telephone number is 571-272-0777.

The examiner can normally be reached on 9:30-6:00 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Celine X Qian Ph.D.  
Examiner  
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**CELIAN QIAN**  
**PATENT EXAMINER**  
